

## REMARKS

### **I. Amendment to the Claims**

By the foregoing amendment to the claims, claim 1 has been amended to recite a temperature range of "30°-60°" as supported at least at page 16 of the present specification.

The amendment to the claims has been made without prejudice or disclaimer to any subject matter recited or canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No new matter has been added, and entry of the foregoing amendment is respectfully requested.

### **II. Response to Claim Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 1, 21-23 and 28 have been rejected under 35 U.S.C. § 112, second paragraph, as purportedly being indefinite for reciting "30°-30°" (claim 1).

As noted above, claim 1 has been amended to recite a temperature range of "30°-60°."

Accordingly, Applicants respectfully request reconsideration and withdrawal of the indefiniteness rejection.

### **III. Response to Claim Rejection Under 35 U.S.C. § 103**

Claims 1, 21-23 and 28 have been rejected under 35 U.S.C. § 103(a) as purportedly being unpatentable over Toshiyuki et al. in view of Yujiro et al., JP 2000-319116 (English Translation). This rejection is respectfully traversed.

The present claims recite a method for preparing a glycoside under conditions where the acetic acid produced as a byproduct is removed at a specific rate and temperature to maintain the concentration of acetic acid in the reaction system at a low level. The Declaration Under 37 C.F.R. § 1.132 of Mr. Akinori Nagatomo, submitted herewith, demonstrates that the recited method provides unexpected results as compared to the closest prior art.

Experiments 1 and 4 in the Declaration correspond to Examples 1 and 6, respectively, in the present specification. Further, Experiment 5 in the Declaration corresponds to Example 1 described in Toshiyuki et al (JP 62-263194). Experiments 2 and 3 in the Declaration further show the disadvantages that result when the reactions are performed under conditions that fall outside the scope of the present claims.

Toshiyuki et al. discloses a process for preparing a hydroquinone derivative glycosidically linked to a sugar through the reaction including removing acetic acid as a byproduct. However, Toshiyuki et al. does not teach or suggest the reaction conditions recited in the present claims, and the process of Toshiyuki et al. is directed only to the preparation of a mono-glycoside compound, not a diglycoside compound.

In Experiment 5 in the Declaration, which as noted above corresponds to the method of Toshiyuki et al., high yields of a mono-glycoside compound were obtained. In contrast, in Experiment 4 in the Declaration, the method recited in the present claims is used to prepare a hydroquinone derivative. The results of Experiment 4 demonstrate that the present method produces high yields of a diglycoside compound, and extremely low yields of mono-glycoside compound were obtained as compared to those of the diglycoside compound.

The difference between the results of Experiments 4 and 5 is clearly due to the reaction conditions, specifically the reaction temperature and the concentration of acetic acid in the reaction system during the reaction.

Experiments 2 and 3 in the Declaration provide further evidence that a mono-glycoside compound is obtained as an main product when the reaction conditions are outside of the scope of the present claims.

The present inventors have discovered that there is an equilibrium between a gallic acid methyl ester (as a starting material), mono-glycoside and diglycoside based on the concentration of the byproduct acetic acid. Surprisingly, the equilibrium will be shifted to produce diglycoside when the acetic acid is removed as recited in the present claims. However, when the concentration of acetic acid is high, the hydroxyl group which should be involved in glycosidation is acetylated so that the diglycoside compound is no longer generated. Thus, the present inventors have discovered that the conditions recited in the claims are surprisingly advantageous.

In contrast to the present invention, the process of Toshiyuki et al. is directed to the production of mono-glycoside in a high yield. Toshiyuki et al. hypothesize that high yields of mono-glycoside are obtained using the reference methods for the following reasons:

- (1) The specific reaction solvent is employed so that the reactant and resulting material are highly soluble, providing a homogeneous reaction system;
  - (2) The acetic acid as a byproduct can be easily removed from the reaction system;
- and

(3) Isomeric transition of the resulting compounds is taking place at an extremely low level.

With respect to (2), Toshiyuki et al. explain that since a reaction solvent having a higher boiling point than acetic acid is employed, the acetic acid can be easily removed from the reaction system, leading to the high yield of mono-glycoside. However, in contrast to the claimed methods, the concentration of acetic acid is not controlled. Therefore, Toshiyuki et al. do not teach or suggest any solutions to the problems related to preparation of diglycoside compounds in particular. In other words, although Toshiyuki et al. disclose methods for preparing glycoside compounds involving removing acetic acid from the reaction system, Toshiyuki et al. do not teach or suggest a temperature range of 30°C to 60°C, nor maintaining the concentration of the acetic acid in the reaction system at 1.0 percent by weight or less during the reaction. Thus, the reference merely discloses methods for preparing mono-glycoside compounds, and does not teach or suggest methods for preparing diglycoside compounds.

If a person of ordinary skill in the art had tried to obtain diglycoside compounds based on the teachings of Toshiyuki et al., such person would not have reasonably predicted that the particular reaction temperatures and acetic acid concentrations recited in the present claims would be successful. Accordingly, the present methods are not obvious over Toshiyuki et al.

Furthermore, the deficiencies of Toshiyuki et al. are not remedied by combining Toshiyuki et al. with Yujiro et al. (*JP2000-319116*). Since only a process for preparing a mono-glycoside compound is disclosed in Toshiyuki et al., the present invention is unexpected even if the teachings of Yujiro et al. are combined with those of Toshiyuki et al.

In the Advisory Action, the Examiner has stated that Experiments 2 and 3 show the reaction system wherein the acetic acid is not removed. Therefore, the Examiner concludes that Applicants have failed to show an unexpected discovery related to the equilibrium between the gallic acid methyl ester, monoglycoside and diglycoside based on the concentration of acetic acid by-product, and the removal of acetic acid under the conditions recited in the present claims.

However, in Comparative Example 2 in the specification, the acetic acid was distilled off from the reaction system to keep the concentration of the acetic acid at 1.21% to 1.25% percent by weight in the reaction mixture during the reaction, which falls outside of the scope of the claimed invention. Further, the yields of gallic acid methyl ester-bis(2,3,4,6-tetra-O-

acetylglucoside) and gallic acid methyl ester-mono(2,3,4,6-tetra-O-acetylglucoside) were 61.5% and 35% (relative to the GM), respectively, thus demonstrating inferior results as compared to the Examples representing the present invention.

Thus, Applicants have shown that the present methods provide unexpectedly beneficial results. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

### CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

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